

Amendment to the Claims:

Please amend the claims as follows:

Please cancel claims 55, 58 to 65, 88, 89, 105, 107 to 113 and 131, without prejudice or disclaimer.

This listing of claims will replace all prior versions, and listing, of claims in the application:

Listing of Claims:

Claims 1 to 65 (canceled)

Claim 66 (currently amended): A method of producing increased yields of an intact heavy and light chain-comprising antibody, wherein the intact antibody comprises a heavy chain variant of an antibody lacking at least one inter-heavy chain hinge region disulfide bond, comprising

(a) expressing in a ~~prokaryotic~~ host cell ~~[[the]]~~ an antibody heavy chain-encoding polynucleotide of claim 55, and a polynucleotide encoding antibody light chains capable of functionally pairing with the antibody heavy chains encoded by the polynucleotide wherein the amount of intact antibody produced from the host cell is increased in comparison to the amount of aggregated heavy chain produced in the host cell,

wherein the polynucleotide encoding the variant heavy chain polypeptide is made by a method comprising:

(i) providing a nucleic acid comprising an antibody lacking at least one inter-heavy chain hinge region disulfide bond;

(ii) modifying the nucleic acid to a variant which encodes an antibody heavy chain polypeptide which cannot form at least one inter-heavy chain hinge region disulfide linkage, wherein the variant hinge region cannot form at least one inter-heavy chain hinge region disulfide linkage because it is modified to lack a cysteine residue present in a corresponding non-variant heavy chain polypeptide by either deletion of the cysteine residue or substitution of the cysteine residue with an amino acid residue not capable of forming an inter-heavy chain disulfide linkage, and the modified or deleted cysteine residue is capable of forming an inter-heavy chain hinge region disulfide linkage when present in the corresponding non-variant heavy chain polypeptide; [[and]]

(b) culturing the host cell under conditions permissive for expression of the heavy and light chain antibody polypeptides and pairing of the heavy and light chain antibody polypeptides, wherein the amount of intact antibody produced in the host cell is at least about 10% greater than the amount of an antibody comprising the corresponding non-variant heavy chain polypeptide expressed under similar culture conditions; and

(c) recovering said intact antibody from the host cell.

Claim 67 (currently amended): The method of claim 66, wherein at least two inter-heavy chain disulfide linkages of the antibody variant heavy chain are eliminated by deletion, or by substitution of the antibody heavy chain sequence with an amino acid residue not capable of forming an inter-heavy chain disulfide linkage.

Claim 68 (currently amended): The method of claim 67 [[66]], wherein all inter-heavy chain disulfide linkages of the antibody variant heavy chain are eliminated by deletion, or by substitution of the antibody heavy chain sequence with an amino acid residue not capable of forming an inter-heavy chain disulfide linkage.

Claim 69 (canceled)

Claim 70 (currently amended): The method of claim 67 [[66]], wherein at least two cysteines are substituted in a said-variant hinge region of the antibody heavy chain lacks at least two of the cysteine residues, wherein each of the at least two cysteine residues are capable of forming an inter-chain disulfide linkage when present.

Claim 71 (currently amended): The method of claim 66, wherein all of the cysteine residues in said variant hinge region are modified or deleted lacks all of the cysteine residues, wherein all of the cysteine residues are capable of forming an inter chain disulfide linkage when present.

Claim 72 (currently amended): The method of claim 66, wherein a cysteine of a ~~[[the]]~~ hinge region is ~~deleted or substituted with another amino acid~~.

Claim 73 (currently amended): The method of claim 66 ~~[[72]]~~, wherein said cysteine residue is ~~substituted with~~ modified to be a serine residue.

Claim 74 (currently amended): The method of claim 66, wherein said antibody heavy chain-encoding polynucleotide encodes ~~[[is]]~~ a full-length antibody heavy chain polypeptide.

Claim 75 (currently amended): The method of claim 66, wherein said antibody heavy chain-encoding polynucleotide encodes a ~~[[is]]~~ humanized heavy chain polypeptide.

Claim 76 (currently amended): The method of claim 66, wherein said antibody heavy chain-encoding polynucleotide encodes a ~~[[is]]~~ human heavy chain polypeptide.

Claims 77 to 78 (canceled)

Claim 79 (currently amended): The method of claim 66, wherein said antibody comprises a human heavy chain constant domain and a human light chain constant domain.

Claim 80 (currently amended): The method of claim 66, wherein said antibody heavy chain is selected from the group consisting of IgG, IgA and IgD.

Claim 81 (currently amended): The method of claim 66, wherein said antibody heavy chain is selected from the group consisting of IgG, IgA, IgE, IgM and IgD.

Claim 82 (previously presented): The method of claim 80, wherein the antibody is IgG.

Claim 83 (previously presented): The method of claim 82, where said antibody is IgG1 or IgG2.

Claim 84 (currently amended): The method of claim 66, wherein said antibody is a selected from the group consisting of therapeutic, an agonist, an antagonist, a diagnostic, a blocking or a [[and]] neutralizing antibody antibodies.

Claim 85 (original): The method of claim 66, wherein heavy and light chains of said antibody are encoded by a single polynucleotide.

Claim 86 (withdrawn): The method of claim 66, wherein heavy and light chains of said antibody are encoded by separate polynucleotides.

Claim 87 (currently amended): The method of claim 66, further comprising determining that the intact antibody having the variant heavy chain polypeptide that is recovered is biologically active or retains binding activity to the same antigen as the antibody having the non-variant heavy chain polypeptide.

Claim 88 to 89 (canceled)

Claim 90 (currently amended): The method of claim 66 ~~[[88]]~~, wherein the amount of intact antibody produced in the host cell is at least about 25% greater than the amount of an antibody comprising the corresponding non-variant heavy chain polypeptide expressed under similar culture conditions.

Claim 91 (currently amended): The method of claim 90, wherein the amount of intact antibody produced in the host cell is at least about 50% greater than the amount of an antibody comprising the corresponding non-variant heavy chain polypeptide expressed under similar culture conditions.

Claim 92 (currently amended): The method of claim 91, wherein the amount of intact antibody produced in the host cell is at least about 75% greater than the amount of an antibody comprising the corresponding non-variant heavy chain polypeptide expressed under similar culture conditions.

Claim 93 (currently amended): The method of claim 66, wherein the intact antibody having the variant heavy chain polypeptide and the reference antibody having the non-variant heavy chain polypeptide have substantially similar antigen binding capabilities.

Claim 94 (currently amended): The method of claim 66, wherein the intact antibody having the variant heavy chain polypeptide and the reference antibody having the non-variant heavy chain polypeptide have substantially similar FcRn binding capabilities.

Claim 95 (currently amended): The method of claim 66, wherein the intact antibody having the variant heavy chain polypeptide and the reference antibody having the non-variant heavy chain polypeptide have substantially similar pharmacokinetic values.

Claim 96 (previously presented): The method of claim 66, wherein said host cell is prokaryotic.

Claim 97 (previously presented): The method of claim 96, wherein said host cell is a gram-negative bacterial cell.

Claim 98 (previously presented): The method of claim 97, wherein said host cell is *E. coli*.

Claim 99 (previously presented): The method of claim 96, further comprising expressing in the host cell a polynucleotide encoding at least one prokaryotic polypeptide selected from the group

consisting of disulfide bond A (DsbA), disulfide bond C (DsbC), disulfide bond G (DsbG) and FkpA.

Claim 100 (withdrawn): The method of claim 99, wherein the polynucleotide encodes both DsbA and DsbC.

Claim 101 (previously presented): The method of claim 98, wherein the *E. coli* is of a strain deficient in endogenous protease activities.

Claim 102 (canceled)

Claim 103 (currently amended): The method of claim 66, wherein said intact antibody having the variant heavy chain polypeptide is recovered from a cell lysate of the host cell.

Claim 104 (currently amended): The method of claim 66, wherein said intact antibody having the variant heavy chain polypeptide is recovered from a culture medium or a [[the]] periplasm of the host cell.

Claim 105 to 132 (canceled)

Claim 133 (new): The method of claim 66, wherein the polynucleotide encoding the variant heavy chain polypeptide further comprises a secretion signal sequence operably linked to the polynucleotide.

Claim 134 (new): The method of claim 133, wherein the secretion signal sequence comprises a prokaryotic secretion signal sequence operably linked to the polynucleotide.

Claim 135 (new): The method of claim 134, wherein the prokaryotic secretion signal sequence is endogenous to a prokaryotic host cell.

Claim 136 (new): The method of claim 66, wherein the host cell is a prokaryotic cell, an *Archaeobacteria* cell, a *Eubacteria* cell, a gram-negative cell or a gram-positive cell.

Claim 137 (new): The method of claim 136, wherein the host cell is an *Escherichia* cell, an *E. coli* cell, a *Bacilli* cell, a *B. subtilis* cell, an *Enterobacteria* cell, a *Pseudomonas* species cell, a *P. aeruginosa* cell, a *Salmonella* sp. cell or an *S. typhimurium* cell, a *Serratia* sp. cell or an *S. marcescans*, a *Klebsiella* sp. cell, a *Proteus* sp. cell, a *Shigella* sp. cell, a *Rhizobia* sp. cell, *Vitreoscilla* sp. cell, or a *Paracoccus* sp. cell.